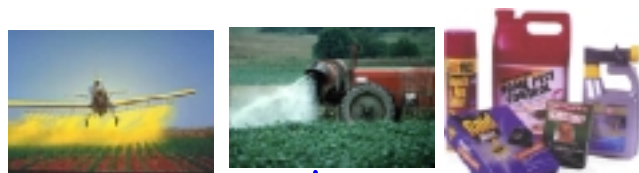


# A Comparative Genomic Approach to Assess the Neurotoxicity of Common Pesticides

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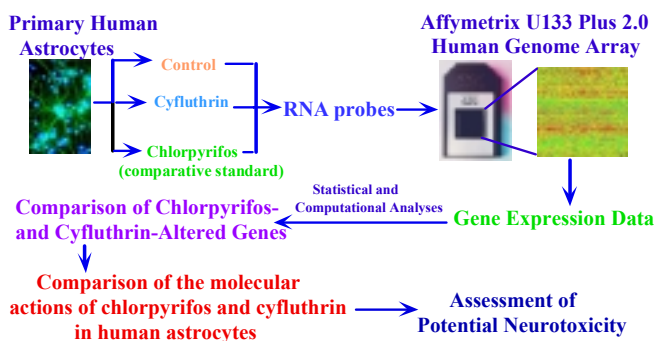
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## 1. Human Exposures to Pesticides Are Ubiquitous



Pesticide Exposures to Developing and Adult Humans

## 2. The Application of Genomic Technology to Compare the Mechanisms Underlying Chlorpyrifos and Cyfluthrin Neurotoxicity



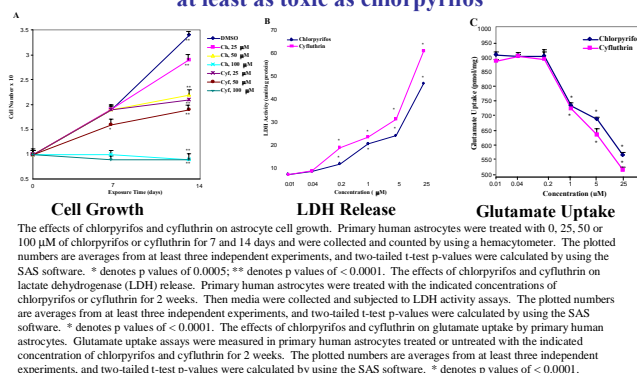
## 3. Data from toxicological analyses are consistent with data from microarray analyses indicating that cyfluthrin is at least as toxic as chlorpyrifos

### A. Both chlorpyrifos and cyfluthrin alter the expression of a group of genes with diverse functions

	Tot (annotated)	Chap	Behav	Dev	Transp	Trans Reg	Sign Trans
Chlorpyrifos	610 (290) < 433+ 177-	5+	5 < 3+ 2-	35 < 22+ 13-	28 < 20+ 8-	24 < 21+ 3-	55 < 41+ 14-
Cyfluthrin	659 (309) < 444+ 219-	3+	5 < 2+ 3-	35 < 26+ 9-	29 < 21+ 8-	34 < 29+ 5-	69 < 49+ 20-

\*The upregulated and downregulated genes in primary human astrocytes (Figure 3) were categorized by using the NIH DAVID annotation program and the Gene Ontology algorithm in GeneSpring. Listed here are the numbers of altered genes encoding functions involved in behavior (Behav) and development (Dev), and those encoding chaperones (Chap), transporters (Transp), transcriptional regulators (Trans Reg) and signal transducers (Sign Trans). The total (Tot) numbers of altered transcripts by chlorpyrifos or cyfluthrin are also shown; the numbers of annotated (classified) genes are shown in parentheses. "+" indicates upregulated genes while "-" indicates downregulated genes.

### B. Toxicological analyses show that cyfluthrin is at least as toxic as chlorpyrifos

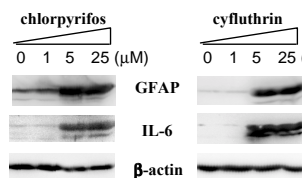


## 4. Both microarray and biochemical analyses suggest that chlorpyrifos and cyfluthrin promote inflammatory activation of human astrocytes

### A. Computational analysis of microarray data shows that targets of the pro-inflammatory interferon- $\gamma$ (IFN- $\gamma$ ) pathway are up-regulated by chlorpyrifos and cyfluthrin



### B. Consistent with results from microarray analysis protein levels of inflammatory factors GFAP and IL-6 are enhanced by pesticide exposure



The effects of chlorpyrifos and cyfluthrin on the protein levels of IL-6, GFAP, p-ERK1/2 and b-actin. Human astrocytes were treated with the indicated concentrations of chlorpyrifos or cyfluthrin as described in Materials and Methods. Then protein extracts were prepared and subjected to Western blotting analysis. The PVDF membranes were probed with polyclonal antibodies against IL-6, GFAP, phospho(Thr202/Tyr204)-ERK1/2 (p-ERK1/2), and b-actin, respectively. Equal amounts of cellular proteins were loaded in every lane, as revealed by the levels of b-actin.

## 5. Conclusion

Cyfluthrin, like chlorpyrifos, may have the potential to cause neurotoxicity in humans. Further studies are necessary to fully assess the neurotoxicity of pyrethroids and other common pesticides.

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